Application no. 10/537,228

Response to Notice to File Corrected Application Papers filed August 18, 2010

Attorney Docket: 14300.1025

Amendments to the Specification:

Kindly amend the paragraph beginning at page 10, line 9, of the specification as originally filed as follows:

Fig. 2 A) Alignment of mouse Ciz1 variants. The predicted full-length Ciz1 amino-acid sequence ('Full') is identical to a mouse mammary tumour cDNA clone (BC018483), while embryonic Ciz1 ('ECiz1', AJ575057), and a melanoma-derived clone (AK089986) lack two discrete internal sequences. In addition, the first available methionine in ECiz1 is in the middle of exon 3 (Met84) which excludes a polyglutamine rich region from the N-terminus. Melanoma derived AK089986 may be incomplete as it ends 77 codons before the C-terminus of all other mouse and human clones. Stars indicate amino-acids changed by site-directed mutagenesis in the constructs shown in D. Amino-acids that correspond to codons targeted by siRNAs are underlined. B) Mouse Ciz1 is encoded by at least 17 exons. Coding exons are shown in grey, alternatively spliced regions are black, untranslated regions are white. Two alternative exon 1 sequences are included in some Ciz1 transcripts (not shown) but an alternative translational start site upstream of the two depicted here has not yet been found. C) Sequence features and putative domains in ECiz1. Predicted nuclear localisation sequence (NLS), putative cyclin-dependent kinase phosphorylation sites, C2H2 type zinc-fingers and a C terminal domain with homology to the nuclear matrix protein matrin 3 (Nakayasu and Berezney, 1991) are shown. The positions of sequences absent from ECiz1 are indicated by triangles. D) ECiz1 and derived truncations and point mutants used in cell-free DNA replication experiments. Numbers in parentheses relate to amino-acid positions in the full-length form of mouse Ciz1, shown in A. Stars indicate putative phosphorylation sites ablated by site-directed mutagenesis.